

## **CLAIMS**

1. A method for increasing Nitric Oxide production in a subject, the method comprising the step of: administering to the subject a HMG-CoA reductase inhibitor in an amount effective to increase Nitric Oxide production in a tissue of the subject.
2. The method of claim 1, wherein the subject is nonhypercholesterolemic
3. The method of claim 1, wherein the subject is nonhyperlipidemic.
4. The method of claim 1, wherein the amount is sufficient to increase Nitric Oxide production above baseline levels.
5. The method of claim 1, wherein the subject has a cytokine-induced condition comprising an abnormally low level of nitric oxide synthase activity.
6. The method of claim 1, wherein the subject has an abnormally elevated risk of pulmonary hypertension.
7. The method of claim 1, wherein the subject has pulmonary hypertension.
8. The method of claim 1, wherein the subject has a condition comprising an abnormally low level of endothelial Nitric Oxide Synthase activity.
9. The method of claim 1, wherein the subject has a cardiovascular disease or disorder or a cerebrovascular disease or disorder.
10. The method of claim 1, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of simvastatin, lovastatin, atorvastatin, pravastatin, cerivastatin, and fluvastatin.

11. The method of claim 1, wherein the HMG-CoA reductase inhibitor is simvastatin.
12. The method of claim 1, wherein the HMG-CoA reductase inhibitor is lovastatin.
13. The method of claim 1, wherein the HMG-CoA reductase inhibitor is pravastatin.
14. The method of claim 1, wherein the HMG-CoA reductase inhibitor is fluvastatin.
15. The method of claim 1, wherein the HMG-CoA reductase inhibitor is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.
16. The method of claim 1, wherein the HMG-CoA reductase inhibitor is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
17. The method of claim 1, further comprising co-administering a substrate of Nitric Oxide Synthase.
18. The method of claim 17, wherein the substrate of Nitric Oxide Synthase is L-arginine.
19. The method of claim 17, wherein the substrate of Nitric Oxide Synthase is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.
20. The method of claim 17, wherein the substrate of Nitric Oxide Synthase is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
21. The method of claim 17, further comprising co-administering a Nitric Oxide Synthase cofactor.

22. The method of claim 21, wherein the Nitric Oxide Synthase cofactor is NADPH or tetrahydrobiopterin.
23. A method for attenuating the downregulation of Nitric Oxide production in a subject, the method comprising the step of: administering to the subject a HMG-CoA reductase inhibitor in an amount effective to attenuate the downregulation of Nitric Oxide production in a tissue of the subject.
24. The method of claim 23, wherein the subject is nonhypercholesterolemic or nonhyperlipidemic.
25. The method of claim 23, wherein the subject has a cardiovascular disease or disorder or a cerebrovascular disease or disorder.
26. The method of claim 23, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of simvastatin, lovastatin, atorvastatin, pravastatin, cerivastatin, and fluvastatin.
27. The method of claim 23, wherein the HMG-CoA reductase inhibitor is simvastatin.
28. The method of claim 23, wherein the HMG-CoA reductase inhibitor is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.
29. The method of claim 23, wherein the HMG-CoA reductase inhibitor is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
30. The method of claim 23, further comprising co-administering a substrate of Nitric Oxide Synthase.

31. The method of claim 30, wherein the substrate of Nitric Oxide Synthase is L-arginine.
32. The method of claim 30, wherein the substrate of Nitric Oxide Synthase is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.
33. The method of claim 30, wherein the substrate of Nitric Oxide Synthase is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
34. The method of claim 23, further comprising co-administering a Nitric Oxide Synthase cofactor.
35. The method of claim 34, wherein the Nitric Oxide Synthase cofactor is NADPH or tetrahydrobiopterin.
36. A method for treating a nonhypercholesterolemic or nonhyperlipidemic subject with a cardiovascular disease or disorder, the method comprising the step of: administering to the subject a HMG-CoA reductase inhibitor.
37. The method of claim 36, wherein the cardiovascular disease or disorder is atrial fibrillation, unstable angina, Prinzmetal's angina, ventricular tachycardia, dilated cardiomyopathy, pulmonary hypertension, coronary heart disease, myocardial infarction, or cardiomegaly.
38. The method of claim 36, further comprising co-administering a second agent.
39. The method of claim 38, wherein the second agent is selected from the group consisting of: cardioprotectants, cardiac depressants, cardiotonics, cerebral ischemia

agents, unstable angina agents, vasoconstrictors, antithrombotics, and cardiovascular agents.

40. The method of claim 36, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of simvastatin, lovastatin, atorvastatin, pravastatin, cerivastatin, and fluvastatin.

41. The method of claim 36, wherein the HMG-CoA reductase inhibitor is simvastatin.

42. The method of claim 36, wherein the HMG-CoA reductase inhibitor is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.

43. The method of claim 36, wherein the HMG-CoA reductase inhibitor is administered in the form of a capsule, tablet, lozenge, or injectable preparation.

44. The method of claim 36, further comprising co-administering a substrate of Nitric Oxide Synthase.

45. The method of claim 44, wherein the substrate of Nitric Oxide Synthase is L-arginine.

46. The method of claim 44, wherein the substrate of Nitric Oxide Synthase is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.

47. The method of claim 44, wherein the substrate of Nitric Oxide Synthase is administered in the form of a capsule, tablet, lozenge, or injectable preparation.

48. The method of claim 36, further comprising co-administering a Nitric Oxide Synthase cofactor.
49. The method of claim 48, wherein the Nitric Oxide Synthase cofactor is NADPH or tetrahydrobiopterin.
50. A method for treating a subject with a cerebrovascular disease or disorder comprising: administering to the subject a HMG-CoA reductase inhibitor.
51. The method of claim 50, wherein the subject is nonhypercholesterolemic or nonhyperlipidemic.
52. The method of claim 50, wherein the cerebrovascular disease or disorder is cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL), neurodegenerative disease, Parkinson's Disease, Huntington's Disease, Alzheimer's Disease, or amyotrophic lateral sclerosis (ALS).
53. The method of claim 50, further comprising co-administering a second agent.
54. The method of claim 53, wherein the second agent is selected from the group consisting of: analeptics, analgetics, anesthetics, adrenergic agents, anti-adrenergic agents, amino acids, antagonists, antidotes, anti-anxiety agents, anticholinergics, anticolvunsants, antidepressants, anti-emetics, anti-epileptics, anti-hypertensives, anti-fibrinolytics, antihyperlipidemics, antimigraines, antinauseants, antineoplastics, antiobessional agents, antiparkinsonian agents, antipsychotics, appetite suppressants, blood glucose regulators, cognition adjuvants, cognition enhancers, dopaminergic agents, emetics, free oxygen radical scavengers, glucocorticoids, hypocholesterolemics, holylipidemics, histamine H<sub>2</sub> receptor antagonists, immunosuppressants, inhibitors, memory adjuvants, mental performance enhancers, mood regulators, mydriatics, neuromuscular blocking agents, neuroprotectives, NMDA antagonists, post-stroke and post-head trauma treatments, psychotropics, sedatives, sedative-hypnotics, serotonin

inhibitors, tranquilizers, agents for the treatment of cerebral ischemia, calcium channel blockers, free radical scavengers - antioxidants, GABA agonists, glutamate antagonists, AMPA antagonists, kainate antagonists, competitive and non-competitive NMDA antagonists, growth factors, opioid antagonists, phosphatidyletholine precursors, serotonin agonists, sodium-and calcium-channel blockers, and potassium channel openers.

55. The method of claim 50, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of simvastatin, lovastatin, atorvastatin, pravastatin, cerivastatin, and fluvastatin.

56. The method of claim 50, wherein the HMG-CoA reductase inhibitor is simvastatin.

57. The method of claim 50, wherein the HMG-CoA reductase inhibitor is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.

58. The method of claim 50, wherein the HMG-CoA reductase inhibitor is administered in the form of a capsule, tablet, lozenge, or injectable preparation.

59. The method of claim 50, further comprising co-administering a substrate of Nitric Oxide Synthase.

60. The method of claim 59, wherein the substrate of Nitric Oxide Synthase is L-arginine.

61. The method of claim 59, wherein the substrate of Nitric Oxide Synthase is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.

62. The method of claim 59, wherein the substrate of Nitric Oxide Synthase is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
63. The method of claim 50, further comprising co-administering a Nitric Oxide Synthase cofactor.
64. The method of claim 63, wherein the Nitric Oxide Synthase cofactor is NADPH or tetrahydrobiopterin.
65. A method for increasing cerebral blood flow in a cerebral tissue of a subject comprising: administering to the subject a HMG-CoA reductase inhibitor in an amount effective to increase Nitric Oxide Synthase activity in the cerebral tissue of the subject.
66. The method of claim 65, further comprising co-administering a second agent to the subject.
67. The method of claim 66, wherein the delivery of the second agent is enhanced by the increased blood flow.
68. The method of claim 66, wherein the second agent is selected from the group consisting of: analeptics, analgetics, anesthetics, adrenergic agents, anti-adrenergic agents, amino acids, antagonists, antidotes, anti-anxiety agents, anticholinergics, anticolvunsants, antidepressants, anti-emetics, anti-epileptics, anti-hypertensives, anti-fibrinolytics, antihyperlipidemics, antimigraines, antinauseants, antineoplastics, antiobessional agents, antiparkinsonian agents, antipsychotics, appetite suppressants, blood glucose regulators, cognition adjuvants, cognition enhancers, dopaminergic agents, emetics, free oxygen radical scavengers, glucocorticoids, hypocholesterolemics, hollylipidemics, histamine H2 receptor antagonists, immunosuppressants, inhibitors, memory adjuvants, mental performance enhancers, mood regulators, mydriatics, neuromuscular blocking agents, neuroprotectives, NMDA antagonists, post-stroke and post-head trauma treatments, psychotropics, sedatives, sedative-hypnotics, serotonin



inhibitors, tranquilizers, agents for the treatment of cerebral ischemia, calcium channel blockers, free radical scavengers - antioxidants, GABA agonists, glutamate antagonists, AMPA antagonists, kainate antagonists, competitive and non-competitive NMDA antagonists, growth factors, opioid antagonists, phosphatidyletholine precursors, serotonin agonists, sodium-and calcium-channel blockers, and potassium channel openers.

69. The method of claim 65, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of simvastatin, lovastatin, atorvastatin, pravastatin, cerivastatin, and fluvastatin.

70. The method of claim 65, wherein the HMG-CoA reductase inhibitor is simvastatin.

71. The method of claim 65, wherein the HMG-CoA reductase inhibitor is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.

72. The method of claim 65, wherein the HMG-CoA reductase inhibitor is administered in the form of a capsule, tablet, lozenge, or injectable preparation.

73. The method of claim 65, further comprising co-administering a substrate of Nitric Oxide Synthase.

74. The method of claim 73, wherein the substrate of Nitric Oxide Synthase is L-arginine.

75. The method of claim 73, wherein the substrate of Nitric Oxide Synthase is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.

76. The method of claim 73, wherein the substrate of Nitric Oxide Synthase is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
77. The method of claim 65, further comprising co-administering a Nitric Oxide Synthase cofactor.
78. The method of claim 77, wherein the Nitric Oxide Synthase cofactor is NADPH or tetrahydrobiopterin.
79. A method for increasing Nitric Oxide Synthase activity in a subject, the method comprising the step of: administering to the subject a HMG-CoA reductase inhibitor and a Nitric Oxide Synthase substrate in an amount effective to increase Nitric Oxide Synthase activity in the subject.
80. The method of claim 79, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of simvastatin, lovastatin, atorvastatin, pravastatin, cerivastatin, and fluvastatin.
81. The method of claim 79, wherein the HMG-CoA reductase inhibitor is simvastatin.
82. The method of claim 79, wherein the HMG-CoA reductase inhibitor is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.
83. The method of claim 79, wherein the HMG-CoA reductase inhibitor is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
84. The method of claim 79, further comprising co-administering a substrate of Nitric Oxide Synthase.

85. The method of claim 84, wherein the substrate of Nitric Oxide Synthase is L-arginine.
86. The method of claim 84, wherein the substrate of Nitric Oxide Synthase is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.
87. The method of claim 84, wherein the substrate of Nitric Oxide Synthase is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
88. The method of claim 79, wherein the HMG-CoA reductase inhibitor and the Nitric Oxide synthase substrate are administered simultaneously.
89. The method of claim 79, wherein the HMG-CoA reductase inhibitor and the Nitric Oxide synthase substrate are administered sequentially.
90. A method for increasing Nitric Oxide production in a subject, the method comprising the step of: administering to a subject a HMG-CoA reductase inhibitor and a second agent.
91. The method of claim 90, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of simvastatin, lovastatin, atorvastatin, pravastatin, cerivastatin, and fluvastatin.
92. The method of claim 90, wherein the HMG-CoA reductase inhibitor is simvastatin.
93. The method of claim 90, wherein the HMG-CoA reductase inhibitor is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.

94. The method of claim 90, wherein the HMG-CoA reductase inhibitor is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
95. The method of claim 90, wherein the second agent is NADPH.
96. The method of claim 90, wherein the second agent is L-arginine.
97. The method of claim 90, wherein the second agent is an antihyperlipoproteinemic.
98. The method of claim 90, wherein the second agent is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.
99. The method of claim 90, wherein the second agent is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
100. The method of claim 90, wherein the HMG-CoA reductase inhibitor and the second agent are administered simultaneously.
101. The method of claim 90, wherein the HMG-CoA reductase inhibitor and the second agent are administered sequentially.
102. A method for treating a subject with an inflammatory disease or disorder comprising: administering to the subject a HMG-CoA reductase inhibitor.
103. The method of claim 102, wherein the subject is nonhypercholesterolemic or nonhyperlipidemic.
104. The method of claim 102, wherein the inflammatory disease or disorder is a rheumatological disease selected from the group consisting of lupus, rheumatoid arthritis, scleroderma, multiple sclerosis, and other autoimmune diseases.

105. The method of claim 102, further comprising co-administering a second agent.

106. The method of claim 105, wherein the second agent is selected from the group consisting of: analeptics, analgetics, anesthetics, adrenergic agents, anti-adrenergic agents, amino acids, antagonists, antidotes, anti-anxiety agents, anticholinergics, anticolvunsants, antidepressants, anti-emetics, anti-epileptics, anti-hypertensives, anti-fibrinolytics, antihyperlipidemics, antimigraines, antinauseants, antineoplastics, antiobessional agents, antiparkinsonian agents, antipsychotics, appetite suppressants, blood glucose regulators, cognition adjuvants, cognition enhancers, dopaminergic agents, emetics, free oxygen radical scavengers, glucocorticoids, hypocholesterolemics, hollylipidemics, histamine H2 receptor antagonists, immunosuppressants, inhibitors, memory adjuvants, mental performance enhancers, mood regulators, mydriatics, neuromuscular blocking agents, neuroprotectives, NMDA antagonists, post-stroke and post-head trauma treatments, psychotropics, sedatives, sedative-hypnotics, serotonin inhibitors, tranquilizers, agents for the treatment of cerebral ischemia, calcium channel blockers, free radical scavengers - antioxidants, GABA agonists, glutarnate antagonists, AMPA antagonists, kainate antagonists, competitive and non-competitive NMDA antagonists, growth factors, opioid antagonists, phosphatidyleholine precursors, serotonin agonists, sodium-and calcium-channel blockers, and potassium channel openers.

107. The method of claim 102, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of simvastatin, lovastatin, atorvastatin, pravastatin, cerivastatin, and fluvastatin.

108. The method of claim 102, wherein the HMG-CoA reductase inhibitor is simvastatin.

109. The method of claim 102, wherein the HMG-CoA reductase inhibitor is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.

110. The method of claim 102, wherein the HMG-CoA reductase inhibitor is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
111. The method of claim 102, further comprising co-administering a substrate of Nitric Oxide Synthase.
112. The method of claim 111, wherein the substrate of Nitric Oxide Synthase is L-arginine.
113. The method of claim 111, wherein the substrate of Nitric Oxide Synthase is administered in a sustained release delivery system, a delayed release delivery system, or a time release delivery system.
114. The method of claim 111, wherein the substrate of Nitric Oxide Synthase is administered in the form of a capsule, tablet, lozenge, or injectable preparation.
115. The method of claim 102, further comprising co-administering a Nitric Oxide Synthase cofactor.
116. The method of claim 115, wherein the Nitric Oxide Synthase cofactor is NADPH or tetrahydrobiopterin.